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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/537,766	06/06/2005	Yasuki Itoh	081356-0242	5454

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EXAMINER	
WALLENHORST, MAUREEN	
ART UNIT	**PAPER NUMBER**
1743	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/537,766	ITOH ET AL.	
	Examiner	Art Unit	
	Maureen M. Wallenhorst	1743	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,10,11,15-17 and 23-28* is/are rejected.

7)☒ Claim(s) *4-9,12-14,18-22 and 29* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/6/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

1. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

2. Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

3. The abstract of the disclosure is objected to because of the inclusion of legal phraseology such as "comprising". In addition, the abstract should be in single paragraph form. Correction is required. See MPEP § 608.01(b).

4. Claims 4-9, 12-14, 18-22 and 29 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from any other multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claims have not been further treated on the merits.

5. Claims 11, 15-17 and 23-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The unit of concentration for PEG recited in claim 11 is indefinite since it is not clear whether the recited percentage concentration is a percentage by weight or a percentage by volume. See this same problem in claim 24.

On line 2 of claim 15, the phrase "the low density lipoprotein" lacks antecedent basis. See this same problem on lines 2-3 of claim 23, on lines 2-3 of claim 25, and on line 2 of claim 27.

On lines 2-3 of claim 25 and on line 2 of claim 27, the phrase "measuring the low density lipoprotein" is indefinite since it is not clear whether the low density lipoprotein measured is the small particle low density lipoprotein or larger particle low density lipoprotein.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1-2, 15 and 17 are rejected under 35 U.S.C. 102(a) as being anticipated by Hirano et al (article from the Journal of Lipid Research, volume 44, 2003).

Hirano et al teach of a method for the quantification of small particle, dense low-density lipoprotein (sLDL). The method comprises the steps of combining a serum sample with a

reagent containing a polyanion and a divalent cation in order to precipitate low-density lipoproteins other than sLDL. The polyanions can be dextran sulfate, phosphotunstate or heparin, and the divalent cations can be magnesium, calcium or manganese. After the sLDL particles are separated from the serum sample, cholesterol and apo-B levels are measured in the sLDL particles. See the abstract and pages 2195, 2200 of Hirano et al. Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

9. Claims 25 and 27-28 are rejected under 35 U.S.C. 102(b) as being anticipated by Sugiuchi (WO 00/17388, English language equivalent is US 6,794,157).

Sugiuchi teaches of a kit for the determination of both HDL and LDL cholesterol that comprises a reagent for aggregating lipoproteins, and a reagent comprising a combination of cholesterol esterase and cholesterol oxidase. The reagent comprising both cholesterol enzymes can be used to measure low-density lipoproteins. The reagent for aggregating lipoproteins is the combination of a divalent metal salt and at least one member selected from the group consisting of heparin, phosphotungstic acid, dextran sulfuric acid and polyethylene glycol (PEG). Therefore, the kit taught by Sugiuchi contains all of the components recited in the kit of instant claims 25 and 27-28, namely a separation agent that includes a polyanion and a divalent cation or a separation agent that includes polyethylene glycol, and a reagent for measuring low-density lipoprotein. See claims 21 and 24-25 in US Patent 6,794,157.

10. Claims 25 and 27-28 are rejected under 35 U.S.C. 102(b) as being anticipated by Miyauchi et al (US patent no. 5,888,755).

Miyauchi et al teach of a kit for determining the amount of cholesterol in a high density lipoprotein that comprises a first reagent for aggregating lipoproteins, and a second reagent comprising cholesterol esterase and either cholesterol oxidase or cholesterol dehydrogenase. The reagent for aggregating lipoproteins is a combination of a divalent metal salt such as magnesium, calcium or manganese, and an aggregating agent chosen from the group consisting of heparin, phosphotungstic acid, dextran sulfuric acid and polyethylene glycol (PEG). The reagent comprising the cholesterol enzymes can be used to measure low-density lipoproteins. Therefore, the kit taught by Miyauchi et al contains all of the components recited in the kit of instant claims 25 and 27-28, namely a separation agent that includes a polyanion and a divalent cation or a separation agent that includes polyethylene glycol, and a reagent for measuring low-density lipoprotein. See claim 9, 13, 15-16 and 19 of Miyauchi et al.

11. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Griffin et al (article from Atherosclerosis, submitted in the Information Disclosure Statement filed on June 6, 2005).

Griffin et al teach of a method for separating small particle low-density lipoprotein from a plasma sample using ultracentrifugation. The ultracentrifugation isolates small particle LDL by using differences in density, and the quantities of cholesterol and protein in the small particle LDL are measured. See the description of this article given on page 1 of the instant specification as known, background art. Since instant claim 1 only calls for a step of separating small particle LDL from other low density lipoproteins in a sample without specifying how the separation is performed, and a measuring cholesterol, triglycerides or proteins in the separated small particle LDL, the teaching of Griffin et al serves to anticipate claim 1.

12. Claims 1-3 and 15-17 are rejected under 35 U.S.C. 102(a) as being anticipated by JP 2003028882 (submitted in the Information Disclosure Statement filed on June 6, 2005).

JP 2003028882 teaches of a method for the measurement of small dense LDL particles in a sample by combining the sample with a reagent comprising a divalent cation such as magnesium, manganese or calcium, a polyanion such as phosphotungstic acid or a sulfuric acid polysaccharide, and a monovalent cation such as sodium, potassium or lithium. By adjusting the concentrations of the divalent cation, polyanion and monovalent cation in the reagent, different lipoprotein fractions are selectively precipitated and measured separately from one another. By using certain concentrations of the divalent cation, polyanoin and monovalent cation, the small particle LDL is suspended or dissolved according to differences in ionic strength, and the small particle LDL is measured by differences in light absorbency. Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

13. Claims 1-3 and 15-17 are rejected under 35 U.S.C. 102(b) as being anticipated by JP 07294532 (submitted in the Information Disclosure Statement filed on June 6, 2005).

JP 07294532 teaches of a method for the fractionation and measurement of low specific gravity serum lipoprotein based upon precipitation of the lipoprotein in the serum with a polyanion such as dextran sulfate, a divalent cation such as calcium, magnesium or manganese, and a monovalent cation such as sodium or potassium. According to page 10 of the instant specification, small particle LDL is defined as LDL with a low specific gravity. JP 07294532 teaches that by adjusting the concentrations of the polyanion, divalent cation and monovalent cation in the reagent, different lipoprotein fractions including small particle LDL can be

selectively and separately precipitated and measured by nephelometry. The cholesterol, triglyceride and protein portions of each lipoprotein fraction can then be separately determined.

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

16. Claims 10-11 and 23-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over JP 07294532 in view of Sugiuchi (WO 00/17388, English language translation is US 6,794,157). For a teaching of both JP 07294532 and Sugiuchi, see previous paragraphs in this Office action.

The primary reference to JP 07294532 fails to teach that the different lipoprotein fractions in a serum sample can be selectively precipitated and measured by combining the serum sample with a reagent comprising polyethylene glycol. However, based upon the combination of JP 07294532 and Sugiuchi, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to substitute polyethylene glycol (PEG) for the polyanion in the composition taught by JP 07294532 used for selectively precipitating

lipoprotein fractions in a serum sample since Sugiuchi teaches that PEG is a known aggregating agent for aggregating lipoproteins in a serum sample that acts equivalently to a polyanion such as dextran sulfate.

17. Claim 26 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sugiuchi (WO 00/17388, English language translation is US 6,794,157) in view of JP 07294532. For a teaching of both Sugiuchi and JP 07294532, see previous paragraphs in this Office action.

The primary reference to Sugiuchi fails to teach that the reagent for aggregating lipoproteins in the kit also includes a monovalent cation therein in addition to the polyanion and the divalent cation. However, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to include a monovalent cation in the aggregating reagent taught in the kit of Sugiuchi since JP 07294532 teaches that a monovalent cation in a composition also including a polyanion and a divalent cation serves to help adjust the ionic strength of the sample.

18. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Please make note of: Wieland et al, Seidel et al, Draeger et al, Sanders, Antwiler, Arbogast and Miyauchi et al (US Patent nos. 5,736,406, 5,691,159 and 6,811,994), which all teach of methods involving the precipitation of lipoproteins from a sample using a composition containing a polyanion and a divalent/monovalent cation therein.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maureen M. Wallenhorst whose telephone number is 571-272-1266. The examiner can normally be reached on Monday-Thursday from 6:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden, can be reached on 571-272-1266. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Maureen M. Wallenhorst
Primary Examiner
Art Unit 1743

mmw

May 4, 2007

Maureen M. Wallenhorst
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